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SUBMISSION OF PRIORITY DOCUMENT

Sir:

Attached herewith please find a certified copy of European Patent Application No. 99305017.8, submitted in connection with the claim for priority under 37 C.F.R. §1.55 for the above-referenced application.

No fee is believed to be necessary for this submission. Should a fee be required, please charge Deposit Account No. 08-2461 accordingly.

Should the Examiner have any questions or comments concerning the above, the Examiner is respectfully invited to contact the undersigned attorney at the telephone number set forth below.

Respectfully submitted,

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Bescheinigung | Certificate | Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécifiée à la page suivante.

Patentanmeldung Nr. | Patent application No. | Demande de brevet n°

99305017.8

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
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Blatt 2 der Bescheinigung
Sheet 2 of the certificate
Page 2 de l'attestation

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REACTOR VESSEL ARRAY

The present invention is related to a reactor vessel array in which a number of (different) physical and/or chemical operations can be performed, either simultaneously or sequentially.

The desire to perform a multitude of operations in a short time is well known to those skilled in the art and a number of systems have been proposed, and some are commercially available, to decrease the time in which, and possibly the size on which physical and/or chemical operations have to be performed. Reference is made, for instance, to the CombiTec System introduced by Argonaut Technologies in which use is made of the so-called Reactor Cassette.

One of the problems still remaining in this rapidly growing area of technology is how to carry out operations which have to be performed either at elevated temperature and/or elevated pressure and/or which require the handling of reactive components, possibly also at elevated temperatures and/or pressures. It has already been proposed in WO 98/36826 (Sinvent AS) to use multi-autoclaves for the combinatorial synthesis of zeolites and other materials which in essence means using a central block containing a number of separated chambers provided with top- and bottom plates and closing mechanisms which can be integrated with the central block

Despite of all efforts thusfar, there is still much room for improvement, in particular with respect to the limited flexibility of the current systems. Also, further developments to increase the multi-functionality of such

multi-reactor systems could well contribute to improved performance.

It has now been found that excellent results can be obtained when using an improved apparatus as to be described hereinbelow. The present invention therefore relates to an apparatus for performing physical and/or chemical operations comprising holding means provided with openings for an array of reactor vessels; reactor vessels positioned totally or partly within the openings, and connecting means capable of connecting the reactor vessels and the holding means, which connection means are located on or in the holding means surrounding the openings in which the reactor vessels are positioned.

In this basic concept an array of any number of reactor vessels, e.g. 4, 6, 12, 24 or even up to 100 or above, can be held in position and subjected to any number of physical and/or chemical operations which are normally carried out in single reactor vessels. The reactor vessels can have any length provided they can be held in place in the holding means in co-operation with the connection means. Since the available reactor volume is of great importance it is one of the advantages of the present apparatus that the reactors can also be longer than the height of the holding means carrying the openings encompassing the reactor vessels. The vessels can be shorter, equal to or longer than the height of the holding means. Preference is given to reactor vessels protruding through the bottom of the holding means as this allows an increase in reactor volume which is highly desirable in short-time, multiple operations. The length of the reactor vessels is determined to some extent by the support capacity provided by the holding/connecting means. It will be appreciated that in conventional multi-autoclave systems the bottoms of the central block also serve as support for the reactors.

The holding means can be composed of any material compatible with the physical and/or chemical operations to be performed, i.e. wood, glass, plastic, steel or the like. Preference is given to holding means composed of steel. Those skilled in the art will know how to choose them depending on the nature of the operation(s) to be performed. Another advantage of the holding means forming part of the apparatus according to the present invention is that they can be rather short compared with the length of the reactor vessels they are holding, taking into account the strength of the connection means. It is also possible to use reactor vessels having different shapes, or shapes differing from the conventional tubular models, for those parts of the reactor vessels being positioned outside the openings in the holding means. For instance, the reactor vessels may be flasks of conical or spherical shapes having their necks fitting the openings in the holding means. This adds to increase the flexibility of the reactor vessel array according to the present invention. It will be clear that when non-tubular reaction vessels are used which are longer than the height of the holding means, they have to be positioned from below the holding means or, if fitted in from above, require the holding means to be turned upside down prior to use.

If desired, the reactor vessels may be provided with inert linings which can either form an integral part of the inside(s) of the reaction vessels or can be in the form of removable linings, for instance, linings made of (chemically) inert materials such as glass or plastic. If the reactor wall is, for instance, made of steel then an inert lining will be useful to prevent contact between an aggressive component and the wall. For instance, when corrosive materials like hydrochloric acid will have to be placed in steel vessels (because of pressure

requirements) an inert lining will be used to protect the reactor wall.

The connection means are preferably located in recesses which are present at the surface or in the holding means. The recesses serve to contain gaskets which provide the actual connection. Suitably, the gaskets are present in recesses located at the surface of the holding means. Good results have been obtained by using O-shaped rings, in particular with O-shaped rings protruding partially above the surface of the holding means.

The recesses can also be present below the surface of the holding means in which case the gaskets may protrude into the openings in which the reactor vessels will be positioned. The recesses may also be formed by holding means consisting of two layered plates of which one contains the recesses whilst the other serves as support or which parts together produce the recesses when placed on top of each other.

The invention will now be illustrated by the following, non-limiting Figures. For ease of reference, only (part of) one member of a reactor vessel array has been drawn in Figures 1-6. It should be understood that such member forms part of any desired array, e.g. a 2x3, a 4x6 or a 10x10 array. Those skilled in the art will understand how to extrapolate the one member drawing to the appropriate array.

In Figure 1, the basic set-up formed by a reactor vessel, a holding plate and connection means is depicted. In this Figure also an embodiment in which an additional support plate is present is depicted.

In Figure 2 an embodiment is depicted in which a solid support plate is present.

In Figure 3 a more detailed overview of the leak-tight configuration of the connecting means is depicted.

In Figure 4 an embodiment is depicted in which the reactor vessel is closed with a septum.

In Figure 5 an embodiment is depicted in which a support plate and a cover plate are forming part of the array.

In Figure 6 an embodiment is depicted in which a pressure relief valve forms part of a member of the array.

In Figure 7 a general overview of an array of 24 reactor vessels, each provided with a pressure relief valve, is depicted.

For ease of reference, similar parts in the various drawings are numbered identically.

In Figure 1 a reactor vessel 1 is positioned in the opening 2 of a holding means 3 (in the form of a plate) which has a tapered recess 4 surrounding the opening 2. The connecting means 5 is in the form of an O-ring which is positioned within the recess 4 and which in the absence of reactor vessel 1 slightly protrudes within the opening 2 and which tightly surrounds reactor vessel 1 when the reactor vessel is present in the holding means 3. The length of the reactor vessel 1is not critical as long as it is held appropriately by the holding means. If desired, the connecting means 5 can be supported by a support plate 6 which can be fastened to the holding means 3 by means of screws 7 to fit holes in the holding means (not shown). Other forms of fastening, e.g. by clamps or bands can also be applied. In this Figure the support plate 6 has an opening 8 matching the opening 2 of holding means 3.

In Figure 2 an embodiment is depicted in which the support plate 6 is integrally supporting the connecting means 5, which for the whole of the array means a solid support plate, provided with screws 7 to fasten it to the holding means.

In Figure 3 a more detailed view is given of the leak-tight sealing obtained by using the O-ring and the support plate. The three areas of contact (a, b and c) ensure a leak-tight connection between the O-ring , the reactor vessel and the support plate.

In Figure 4 an embodiment is depicted in which the top of the reactor vessel 1 is secured by a septum 9 which is held in place by the support plate 6 having an opening 8 (as depicted in Figure 1) in which septum 9 is positioned. It is possible to provide space at the part of the support plate 6 facing the surface of the holding means 3 in which the edges of septum 9 protrude (and reinforce the leak-tight connection when support plate 6 is fastened to the holding means).

In Figure 5 an embodiment is depicted in which a cover means 10 (in the form of a cover plate) is positioned having an opening 11 of which the diameter matches the diameter of the opening 2 of holding means 3 in which opening septum 9 is positioned. It is possible to provide space at the part of the cover plate 10 facing the surface of the holding means 3 in which the edges of septum 9 protrude (and further reinforce the leak-tight connection when cover plate 10 is fastened to the holding means 3, for instance by screws 12 fitting holes in the holding means).

In Figure 6 an embodiment is depicted in which in stead of a septum a pressure relief valve is positioned at the top of the reactor vessel. The reactor vessel 1 is positioned in the opening 2 of holding plate 3 which has a tapered recess 4 surrounding opening 2.The connecting means 5 is in the form of an O-ring which is positioned within the recess 4. The leak-tight connection is provided by support plate 6 which is fastened to holding means 3 by means of screws 7. Support plate 6 is provided with opening 8 which is dimensioned in such a way that a

pressure relief valve 13 can be positioned above reactor vessel 1 and surrounds opening 8 of support plate 6 thereby allowing a closed reactor space formed by reactor vessel 1 and opening 8. Normally, pressure relief valve 13 will be connected to support plate 6 by means of a screw connection 14.

In Figure 7 an overview is given of an array containing 24 reactor vessels each fitted with a pressure relief valve as described in Figure 7. An array containing 24 reactor vessels 1′ is built up by holding means 3′ having openings through which the bottoms and tops of reactor vessels 1′protrude. A support plate 6′ is providing assistance in keeping the reactor vessels 1′ in place (using O-ring connecting means (not shown) and is fastened to the holding means by screws 7′. The reactor vessels are each fitted with pressure relief valves 13′ fitted to the support plate by screw connections 14′ (not shown).

The reactor vessels are kept in place by connecting means which are preferably located in recesses in the surface of the holding means. Suitably, the connection means are in the form of gaskets. The recesses can have any suitable shape to fit the actual connecting means. They may be tapered (in the direction of the openings), curved or profiled in order to match the actual connecting means. Compressible materials, preferably also capable of deforming, can suitably be applied. For instance, rings or springs made of compressible materials such as rubbers or plastics can be applied but also metal rings or springs (e.g. made of copper or compressible alloys). Good results can be obtained by using so-called O-rings. Such rings are made of compressible and preferably deformable materials such as rubber and preferably protrude to some extent into the openings of the holding means in the absence of reactor vessels. When

reactor vessels are placed within the holding means the O-rings will be retracted when inserting the reactor vessels to the extent that they will surround the openings holding the reactor vessels.

In order to provide the array with more rigidity it is possible to use support plates which are placed on top of the holding means and which are fastened to the holding means by conventional fastening means such as screws, clamps or bands. In one embodiment the support plate is a solid plate covering the total surface of the holding means and the tops of the openings in which the reactor vessels are fitted (their tops being on the same level as the surface of the holding means). In an other embodiment the support plate is provided with openings having diameters matching the diameters of the openings of the holding means so as to allow access to the reactor vessels for performing physical and/or chemical operations. From an accessibility point of view it is preferred to have the diameters of the openings in the support plate matching the diameters of the openings of the holding means. From a support point of view, it is preferred to reduce the weight of the support plate by having a number of notches or holes in the support plate. They can be of any size and/or shape as long as they serve to provide adequate support.

It will be clear that the openings can have any suitable shape and need not necessarily to be circular; the can be of oval or lobed shape, though preference is given to circular openings. The holes trough the holding plate can be vertical or tilted. Preference is given to vertical or substantially vertical openings, in particular of cylindrical shape as that set-up is most common and allows a large deal of flexibility.

An important aspect of operating an array of reactor vessels at elevated temperature and pressure is to be

able to perform the desired operation(s) under leak-tight conditions. This can be achieved in the array system according to the present invention when use is made of the connecting means together with a cover means which is removably fitted to the holding means when use is made of a gasket, in particular an O-ring type gasket which is dimensioned such that - in the absence of a reactor vessel - its height protrudes to some extent above the surface of the holding means. When the reactor vessel is present in the opening and kept there by means of the O-ring and a support plate and/or the cover plate (either solid or containing a septum or another form of closure) is present as well, a leak-tight sealing has been achieved.

As such the support plate can serve as cover means to the extent that it indeed effectively closes off the openings in the holding means in which the reactor vessels are fitted. Effective closing will also be achieved when use is made of a solid support plate (fastened as appropriate to the holding means) or by a support plate containing openings having diameters equal to or smaller than the diameters of the openings of the holding means they are matching provided these openings are closed with materials operating as a permeable (though leak-tight) seals for the top of the reactor vessels.

It is also possible in another embodiment of the apparatus according to the present invention to have a cover means (on top of the support plate) on top of the holding means. The cover means can be in the form of a solid plate but is preferably in the form of a plate as described hereinbefore, in particular with respect to the size of the openings. In a preferred embodiment, the apparatus according to the present invention has a cover means composed of a solid plate having opening of which

the diameters match at most the diameters of the openings of the holding means whilst septa covering the tops of the reactor vessels are present between the surface of the holding means and that of the cover means. In a further embodiment of the apparatus according the present invention the septa are located above the reactor vessel and between the support plate and the cover means so as to create a leak-tight volume composed of the reactor vessel and the openings within the support plate and the cover means to the extent that the latter is neighbouring to the side of the septum facing the top of the reactor vessel.

The reactor vessel array according to the present invention can be operated at pressures in the range of from 0 to 200 bar, preferably in the range of from 0 to 50 bar, whilst maintaining leak-tight conditions. The operations can be carried out at ambient temperature (or below) and also at elevated temperatures depending on the type of operation envisaged. Those skilled in the art will now how to select the appropriate temperature and pressure conditions.

It is an important aspect of the apparatus according to the present invention (adding to its flexibility) that the cover means, and optionally, the support plate, can be provided with openings to allow certain physical and/or chemical operations to be performed. This is the case not only in operations which can be carried out at normal (or elevated) temperature and at atmospheric pressure in open systems but even more so in operations requiring closed, though accessible, volumes of reactor space.

For instance, the use of cover means provided with openings as defined hereinbefore allows performing certain types of physical and/or chemical operations either simultaneously or sequentially without having to

dissemble the apparatus to a large extent or even at all. For instance, in stead of a septum (which of course can act as a layer through which liquid(s) can be added or withdrawn, the closure of the reactor vessel can be effected by means of a pressure relief valve which widens the window of opportunities, in particular with respect to carrying out reactions which require pressure. Other options which are possible within the concept of the top of the reactor vessel being covered whilst being capable of performing other duties comprise the presence of condensing means (thereby allowing for instance reflux-type operations being carried out in array systems), filtration means, manifolds and stirring means.

When stirrer means form part of the apparatus according to the present invention they can be operated by means of shafts connected to a central motor so that the array is operated with the same stirrer speed and energy input for the individual members of the array.

The present invention also encompasses processes for performing physical and/or chemical operations to be carried out in an apparatus as envisaged by the present invention. Examples of physical processes which can be performed in the apparatus according to the present invention are mixing, centrifugation and evaporation.

When mixing is to be performed as a process using the apparatus according to the present invention as a means to carry out the process, use can be made of an orbital shaker, i.e. a piece of equipment designed to shake or rotate a number of reactor vessels at the same time. Such devices are commercially available and those skilled in the art will know when to apply such equipment. Sometimes, it will appear that the use of an orbital shaker, even at relatively high speed is not enough to achieve the envisaged mixing operation. In such event it can be advantageous, in particular when dealing with

rather viscous systems, to provide each reactor vessel in the array with an individual stripper, for instance a rod-like stirrer which will provide additional stirring capacity to the mixture being already in movement by operating the orbital shaker.

In an other embodiment of the process according to the present invention, use is made of ultra-sound facilities to cause mixing in an array of reactor vessels. To that extent, the array of reactor vessels can be placed conveniently in a bath capable of producing ultra-sound. Such devices are known in the art.

In yet another embodiment of the process according to the present invention, the array of reactor vessels can be put as such in a centrifuge in order to perform a centrifugal operation. Like wise, the array of reactor vessels can be placed within a unit designed to evaporate, for instance by initiating and maintaining a reduced pressure in the unit in which the array has been placed.

Also heating and cooling are processes (which can be either of physical or of chemical nature) which can be operated smoothly when an array of reactor vessels is place inside the appropriate equipment to carry out heating or cooling operations.

It will also be clear that several operations, for instance mixing and heating, can be carried out simultaneously, again adding to the flexibility of the system in accordance with the present invention. Those skilled in the art know which operations can be combined in order to obtain a better performance, time-wise or otherwise.

The apparatus according to the present invention will be operated in a similar way as far as the unit operations are concerned (mixing, heating etc.) but has, of course, the intrinsic capability that the operations

to be performed within the individual volumes of the reactor vessels need not be the same. Therefore, the apparatus contributes to obtaining information from nearly identical, yet slightly different, process conditions, or, if desired, from rather different process conditions. It is also possible to have certain types of operations identical and others slightly, or even completely, different. Therefore, the apparatus according to the present invention can be instrumental in e.g. rapid catalyst screening but also in combinatorial chemistry. Many of the operations envisaged can be carried out by using robotic means as often practised in combinatorial drug synthesis and screening.

C L A I M S

1. An apparatus for performing physical and/or chemical operations comprising holding means provided with openings for an array of reactor vessels; reactor vessels positioned totally or partly within the openings, and connecting means capable of connecting the reactor vessels and the holding means, which connection means are located on or in the holding means surrounding the openings in which the reactor vessels are positioned.

2. An apparatus according to claim 1, in which the connection means are located in recesses located in or at the surface of the holding means.

3. An apparatus according to claim 1 or 2, in which the recesses are tapered in the direction of the openings.

4. An apparatus according to one or more of claims 1 to 3, in which the connection means are gaskets composed of compressible materials.

5. An apparatus according to claim 4, in which the connection means are in the form of O-shaped rings.

6. An apparatus according to one or more of claims 1-5, in which the connection means are reinforced by the presence of a support plate containing openings having diameters substantially matching the diameters of the openings in the holding means and being removably fitted to the holding means.

7. An apparatus according to claim 6 in which the openings of the support plate match the openings of the holding means and are provided with notches and/or holes to reduce its weight.

8. An apparatus according to one or more of claims 1-5, in which the connection means are in the form of gaskets which together with a cover means for the array of

reactor vessels are capable of creating a leak-tight seal when the cover means is removably fitted to the holding means.

9. An apparatus according to claim 8, in which the gaskets are in the form of O-rings which together with a cover means for an array of cylindrical reactor vessels are capable of creating a leak-tight seal when the cover means is removably fitted to the holding means.

10. An apparatus according to claim 8, in which the cover means comprises a solid plate on top of the surface of the holding means.

11. An apparatus according to claim 10, in which the cover means comprises a plate matching the openings of the holding means whilst the openings of the cover means are closed with permeable material.

12. An apparatus according to claim 8, in which the cover means is composed of a solid plate having openings matching at most the diameters of the openings of the holding means whilst septa covering the tops of the reactor vessels are present between the surface of the holding means and said cover means.

13. An apparatus according to claim 8, in which the cover means comprises a plate having openings having diameters matching at most the diameters of the openings of the holding means, the openings being provided with pressure relief valves.

14. An apparatus according to claim 8, in which the cover means comprises a plate having openings having diameters of at most the diameters of the openings of the holding means, the openings being provided with condensing means.

15. An apparatus according to claim 8, in which the cover means comprises a plate having openings having diameters matching at most the diameters of the openings of the holding means, the opening being provided with filtration means.

16. An apparatus according to claim 8, in which the cover means comprises a plate having openings having diameters matching at most the diameters of the openings of the holding means, the openings being provided with manifolds.

17. An apparatus according to claim 8, in which the cover means comprises a plate having openings having diameters matching the openings of the holding means, the openings being provided with stirrer means.

18. An apparatus according to claim 17, in which the stirrer means are provided with shafts allowing them to be operated by a central motor.

19. An apparatus according to one or more of the preceding claims, in which the reactor vessels are made of glass or steel.

20. An apparatus according to claim 19, in which the bottoms of the reactor vessels protrude through the bottom of the holding means.

21. An apparatus according to one or more of the preceding claims, in which the holding means are made of steel.

22. An apparatus according to claims 6 or 7, in which the support plate is made of the same material as the holding means.

23. An apparatus according to one or more of claims 8-22, in which the cover means is made of the same material as the holding means.

24. An apparatus according to claim 23 or 24, in which the support plate or the cover means are made of the same material as the holding means.

25. A process for performing physical and/or chemical operations in which use is made of an apparatus according to one or more of the preceding claims.

26. A process according to claim 25, in which a mixing operation is performed in which use is made of an orbital shaker.

27. A process according to claim 26, in which use is made of rod-shapes stirrers present in the reaction vessels during mixing.

28. A process according to claim 25, in which a mixing operation is performed in which use is made of ultra-sound to initiate and maintain mixing.

29. A process according to claim 25, in which a heating operation is performed.

30. A process according to claim 29, in which the heating operation is performed together with a mixing operation.

31. A process according to claim 30, in which a cooling operation is performed.

32. A process according to claim 25, in which a centrifugal operation is performed.

33. A process according to claim 25, in which an evaporation operation is performed.

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A B S T R A C T

REACTOR VESSEL ARRAY

An apparatus for performing physical and/or chemical operations comprising holding means provided with openings for an array of reactor vessels; reactor vessels positioned totally or partly within the openings, and connecting means capable of connecting the reactor vessels and the holding means, which connection means are located on or in the holding means surrounding the openings in which the reactor vessels are positioned. Processes which can be carried out with the apparatus comprise, inter alia, mixing, cooling, heating, centrifugation, evaporation, filtration and pressure processes.

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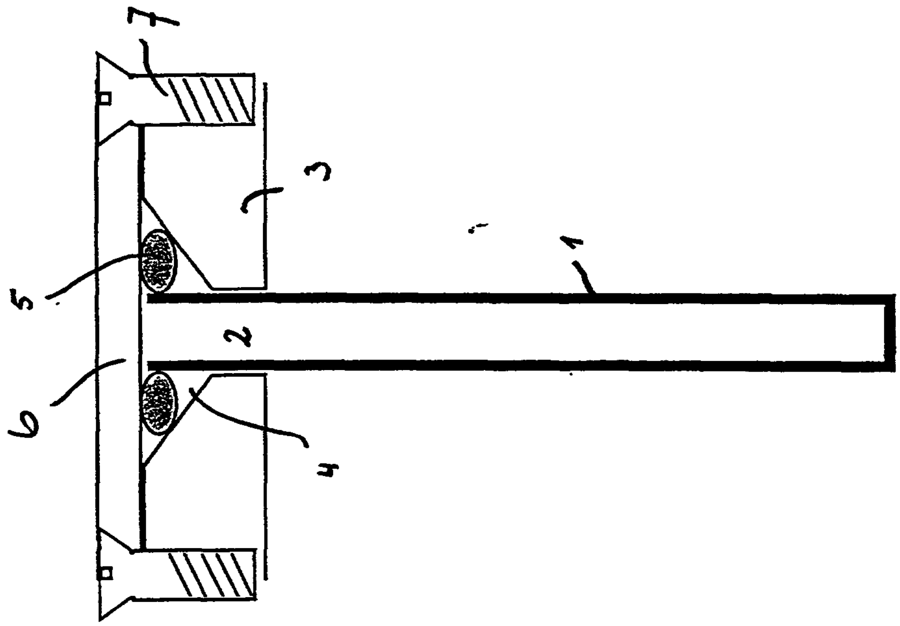

Fig. 2

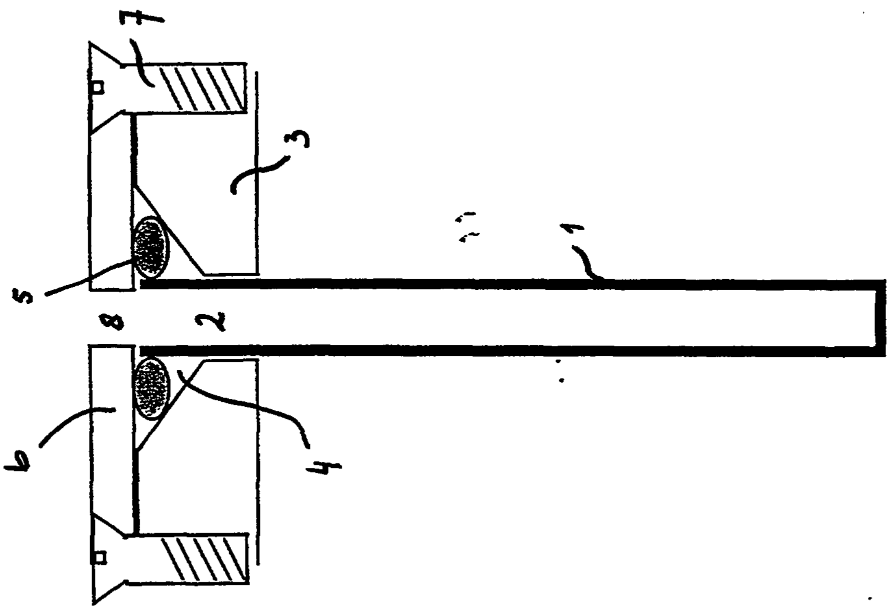

Fig. 1

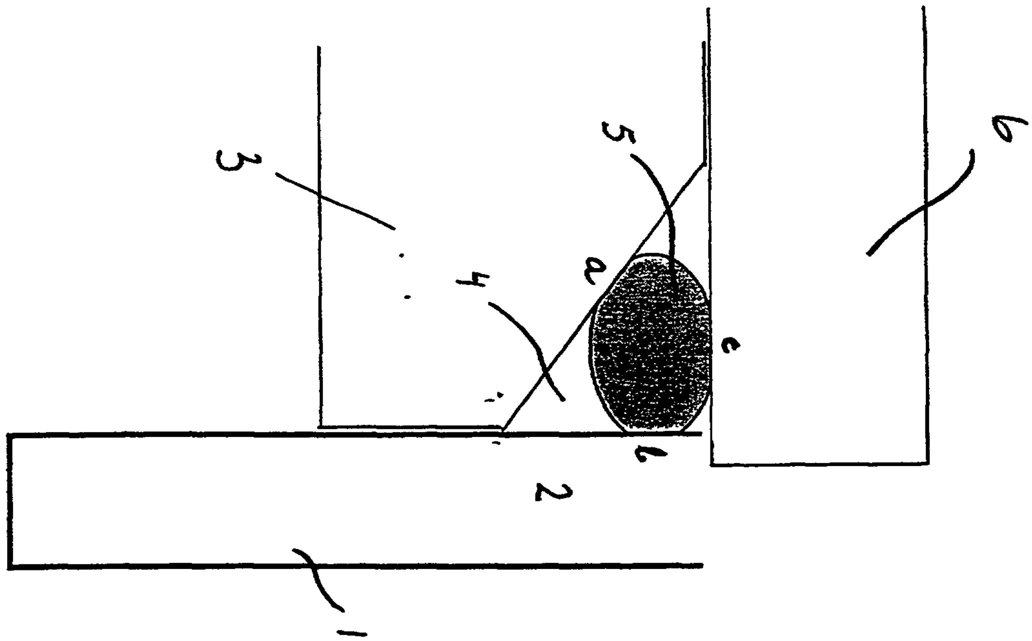

Fig. 3

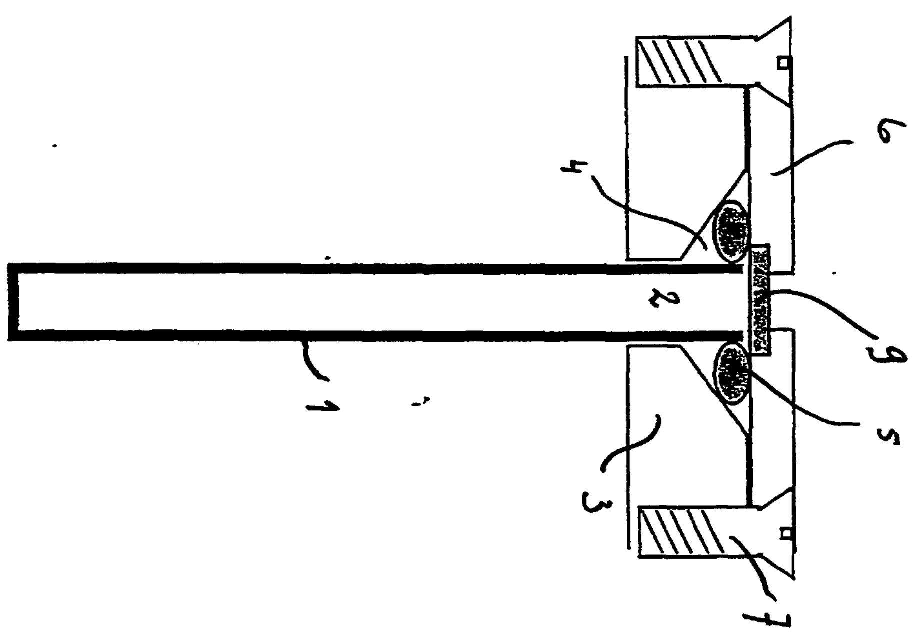

Fig. 4

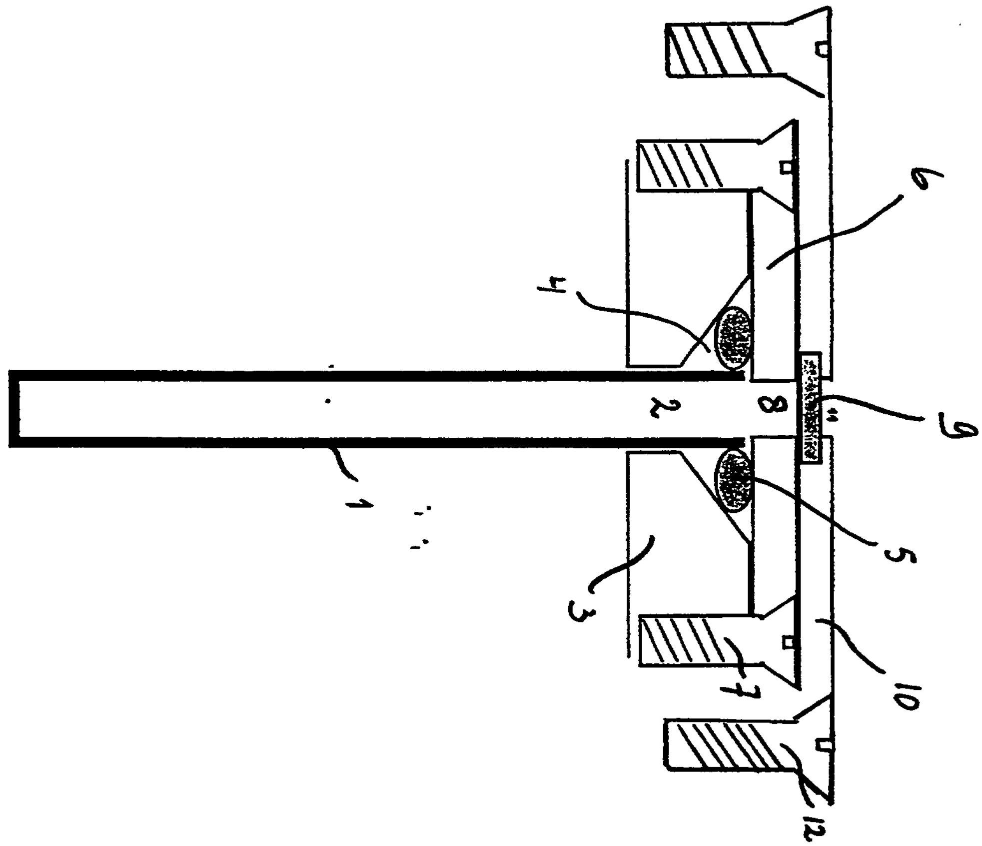

Fig. 5

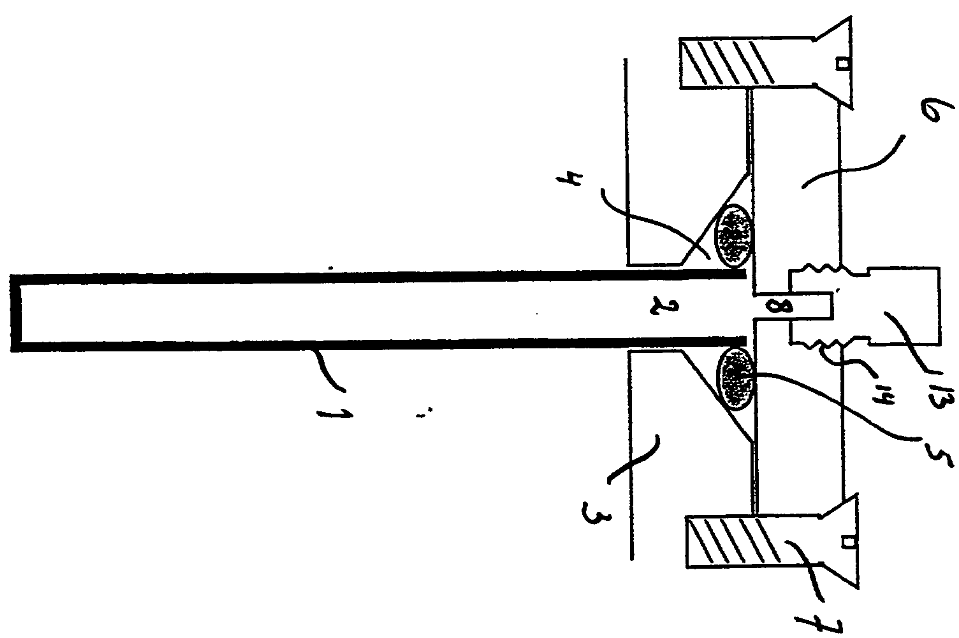

Fig. 6

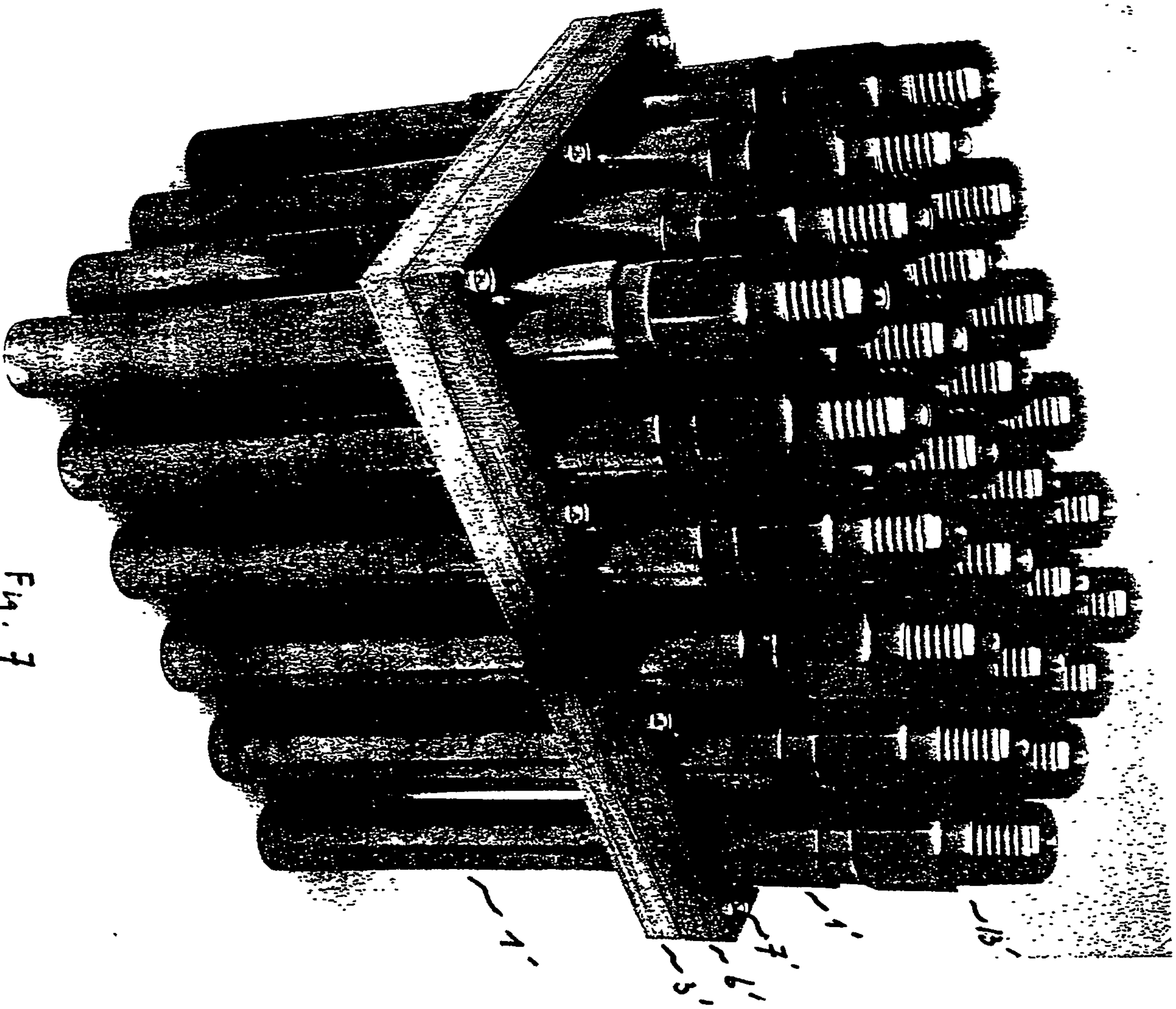

Fig. 7